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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/726,883	11/30/2000	Paul E. Harris	62682/JPW/PT	1468

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EXAMINER
EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
1644	7

DATE MAILED: 07/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/726,883	Harris et al.
Examiner	**Art Unit**
G.R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 29, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-12* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election with traverse of Group II, Claims 1-12, in Paper No. 6, is acknowledged. Applicant's traversal is on the grounds that the inventions of Groups I and II are not independent and distinct and thus, must be examined together.

This is not found persuasive for the following reasons. While the inventions of Groups I and II may not be independent, they are distinct as defined by the MPEP § 802.01 as being "patentable over each other". MPEP § 803 further states that independent and distinct is to be considered independent *or* distinct for restriction purposes. Restriction between patentably distinct inventions can be proper even if said inventions are considered dependent, if undue search burden is established. While it has been noted that the Groups are classified in the same class and subclass, in the establishment of search burden, classification of subject matter is merely one indication of the burdensome nature of the search involved. In the biotechnological arts, the literature searches are generally far more important in evaluating burden of search. In the instant application, the literature searches for the Groups are not coextensive because of the recitation of additional method steps in the invention of Group II. Clearly, different searches and different issues are involved in the examination of each group.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-12, as they recite a method comprising steps (a)-(h) of Claim 8 are being acted upon.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

A) the "dendritic cell culture medium" of Claim 7 has not been defined in the specification. Note that the third paragraph of page 8 of the specification discloses "a" (indicating others exist) dendritic cell culture medium, further, said medium

consists of just three components which are disclosed only as "e.g." (indicating that the disclosed concentrations are only for example only and not defining). Thus, the claims recite a specific method, i.e., "reproducibly generating dendritic cells" employing a specific composition, i.e., "dendritic cell culture medium", said composition however, has not been defined, rendering the claims vague and indefinite.

B) the recitation of "incubating for a predetermined time period tissue culture" in Claims 1, 2, and 8 comprises an ungrammatical phrase of unclear meaning. As such, the claims are considered vague and indefinite.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

The instant invention is drawn to a method of "reproducibly generating dendritic cells" comprising a method of cell culture. Note that the *in vitro* generation of dendritic cells was well known in the art at the time of the invention of the instant claims, however, performing the steps of the instant claims would not necessarily result in a product consisting of said cells given the breadth of the claims, i.e., the lack of specific limitations. As such, the method of the instant claims must be considered highly unpredictable and requiring of undue experimentation.

Step (a) recites the loading of "blood mononuclear cells" into a cell culture container. The specification, however, discloses that it is a "requirement" that the method of the instant claims begin with monocytes and monocyte precursors separated from lymphocytes (page 5, paragraph 4). As such, the method of the instant claims would be highly unpredictable given that the recitation of "blood mononuclear cells" would include lymphocytes in the starting material.

Step (b) recites "incubating for a predetermined time period", however a specific time period is not disclosed. Given that Step (c) requires "separating adherent and nonadherent cells", the incubation time period is a critical feature of the claimed method. U.S. Patent No. 5,851,756 (Example 1) teaches that, depending on the length of incubation, dendritic cells are either nonadherent, loosely adherent, or adherent. As such, the recitation of "incubating for a predetermined time period" alone (without the recitation of any specific time period) renders the method of the instant claims highly unpredictable as it would be unknown whether the method encompassed the further culture (in Step (f)) of the adherent or the nonadherent cells.

Further regarding Step (c) in Claim 1 and Step (d) in Claim 2, and the recitation of "separating nonadherent cells and cells adhered to the beads", Claims 1 and 2 fail to indicate which group of cells is used to generate dendritic cells. As such, the method of the claims must again be considered highly unpredictable because it would appear that the method intends the further culture of one group of cells and the discarding of the other group, but the claims fail to indicate which group is saved and which group is discarded.

Step (f) recites "incubating the container for a second predetermined time period", again however, a specific time period is not disclosed. As the "predetermined time period" is not disclosed, the method must again be considered highly unpredictable as too short a period (e.g., hours) would not result in the generation of dendritic cells, while too long a period (e.g., months) would result in a dead culture. See U.S. Patent No. 5,851,756 (Example 1) which teaches an optimal incubation period of several days.

Further regarding the incubation of the blood mononuclear cells of the instant claims, the generation of dendritic cells from said blood mononuclear cells would require the inclusion of

specific reagents in the incubation, at minimum GM-CSF (in all dendritic cell cultures) and TGF-β (in human dendritic cell cultures), see U.S. Patent No. 5,851,756 (column 14, lines 34-35 and Figure 18) and Strobl et al. (1998, Abstract), respectively.

Regarding the method of Claim 12, wherein a ratio has a value sufficient to hold enough media for incubation, the specification fails to disclose what values would be considered sufficient. As recited, the value would encompass a surface area ranging from that of the container alone (no microcarrier beads), to a container packed full of microcarrier beads. It is unclear, however, if either of said values would allow for the reproducible generation of dendritic cells. Thus, the method of the instant claim must be considered highly unpredictable and requiring of undue experimentation.

As set forth in the previous paragraphs, it is here established that simply performing the method of the instant claims, as broadly claimed, would not result in the "reproducible generation of dendritic cells. As such, the method of the instant claims must be considered highly unpredictable and requiring of undue experimentation. Said undue experimentation in turn indicates that the specification fails to adequately disclose how to make and use the invention of the instant claims.

It is noted that the specification discloses no actual data demonstrating the method of the instant claims, i.e., no working examples. While working examples are not required, given the unpredictable nature of the methods encompassed by the breadth of the instant claims, some demonstration that the method would function in its breadth is required. Said demonstration would in particular address the internal contradictions, e.g., the disclosure that the method must begin with monocytes or monocyte precursors while the claims recite the use of blood mononuclear cells, and said demonstration would additionally address the lack of any recitation of required culture conditions, e.g., the generation of dendritic cells from blood mononuclear cells without culturing under specific conditions, e.g., in GM-CSF. Absent said demonstration, the method of the instant claims must be considered to require undue experimentation.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In view of the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, and the

breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday and alternate Fridays from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The CM1 Fax Center telephone number is (703) 305-3014.

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
July 9, 2002